

**REMARKS**

Claims 1-21 were pending in the application. Claims 1, 3, 4, 5, 7, 9, 10, 12, and 15 have been amended and claim 2 has been canceled. Accordingly, upon entry of the present amendment, claims 1 and 3-21 will remain pending in the application.

Support for the amendments to the claims may be found throughout the specification and claims as originally filed. Specifically, support for the amendments to claim 1 to recite “a DNA methylase” may be found in originally filed claim 2. *No new matter has been added.*

Any amendments to and/or cancellation of the claims are not to be construed as an acquiescence to any of the rejections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

***Request for Reconsideration of Finality of Office Action***

Applicants respectfully traverse the finality of the rejections made in the Final Office Action dated June 27, 2006. Applicants submit that the finality of the present Office Action is improper because the Examiner has introduced new grounds of rejection not necessitated by Applicants’ claim amendments filed during the period set forth in 37 C.F.R. § 1.97(c) (see, MPEP § 706.07(a)). Specifically, the Examiner has finally rejected claims 1-3 and 5-8 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. However, this rejection could have previously been raised by the Examiner and was not necessitated by Applicants’ claim amendments presented in the Amendment and Response of April 3, 2006. As such, the finality of the present Office Action is improper. Applicants, therefore, have been deprived of a sufficient opportunity to respond to this new rejection raised in the Final Office Action and, thus, respectfully request that the finality of the present Office Action be withdrawn.

***Withdrawal of Certain Objections/Rejections***

Applicants gratefully acknowledge the Examiner’s indication that the following objections/rejections have been withdrawn:

the objection to claims 4 and 10 for the recitation of “an Xba1” and “Xba1”;

the objection to claim 6 for the recitation of “claims 1 to 4”;

the objection to claim 9 for the typographical error “io” in step a);

the objection to claim 15 for the typographical error “in to”;

the objection to claim 17 for the recitation of “polyketide synthesising enzyme domain DNA sequences”;

the rejection of claim 1 under 35 U.S.C. §112, second paragraph as being indefinite as to the relationship between the restriction site on the 3’ end of each DNA unit and a recognition site for a DNA modification enzyme;

the rejection of claim 1 under 35 U.S.C. §112, second paragraph as being indefinite for the recitation of “the desired DNA unit” in step c) of the claim;

the rejection of claim 1 under 35 U.S.C. §112, second paragraph as being indefinite for the recitation of “the ligated product” in step c) of the claim;

the rejection of claim 1 under 35 U.S.C. §112, second paragraph as being indefinite for the recitation of “the inserted DNA unit” in step c) of the claim;

the rejection of claim 3 under 35 U.S.C. §112, second paragraph as being indefinite for the recitation of “dam methylase” in the claim;

the rejection of claim 4 under 35 U.S.C. §112, second paragraph as being indefinite as to how to recover a resulting plasmid since step b) ;

the rejection of claim 6 under 35 U.S.C. §112, second paragraph as being indefinite I the recitation of ‘the fragment’ in the claim;

the rejection of claim 8 under 35 U.S.C. §112, second paragraph as being indefinite as to how to replicate the ligated product in a dam- strain of *E. coli* by means of a suitable vector;

the rejection of claim 13, under 35 U.S.C. §112, second paragraph as being indefinite as to how the solid phase is split and mixed; and

the rejection of claim 15, under 35 U.S.C. §112, second paragraph as being indefinite as to a host capable of expressing the protein encoded by the vector.

***Sequence Rules Compliance***

Applicants gratefully acknowledge the Examiner's indication that the Sequence Listing filed on April 3, 2006 complies with the requirements of 37 C.F.R. §1.821-§1.825.

***Drawings***

Applicants gratefully acknowledge the Examiner's indication that Figures 6, 13, and 14 submitted on April 3, 2006 have been accepted by the office.

***Objections to the Specification***

The Examiner has objected to the specification as containing several informalities.

Applicants respectfully submit that the specification has been amended according to the Examiner's suggestions and, accordingly, Applicants respectfully request reconsideration and withdrawal of this objection to the specification.

***Objections to the Claims***

The Examiner has objected to claim 12 because, according to the Examiner, "'the solid phase' should be 'a solid phase'".

Applicants have amended claim 12 according to the Examiner's recommendations. Accordingly, reconsideration and withdrawal of this objection to claim 12 is respectfully requested.

The Examiner has objected to claims 7 and 15 because, according to the Examiner, "'the protein' should be 'a protein'".

Applicants have amended claims 7 and 15 consistent with the Examiner's suggestions to recite "a protein." Accordingly, reconsideration and withdrawal of this objection to claims 7 and 15 is respectfully requested.

***Rejections of Claims 1-3 and 5-8 Under 35 U.S.C. §112, First Paragraph***

The Examiner has rejected claims 1-3 and 5-8 under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. In particular, the Examiner is of the opinion that

the specification, ***while being enabling for performing the methods 1-3 and 5-8 using certain kind of DNA methylase when the DNA unit and the starting DNA construct are cleaved with an identical restriction enzyme***, does not reasonably provide enablement for performing the methods 1-3 and 5-8 using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible restriction enzymes are different restriction enzymes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. (Emphasis added).

With respect to the amount of direction or guidance presented and the predictability or unpredictability of the art, the Examiner is of the opinion that

there is no direction or guidance in the specification to show that the methods 1-3 and 5-8 can be performed using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible restriction enzymes are different restriction enzymes. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods 1-3 and 5-8 can be performed using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible restriction enzymes are different restriction enzymes.

Applicants respectfully traverse the foregoing rejection for the reasons set forth below. As amended, claim 1, and claims dependent therefrom, are directed to methods of assembling several DNA units in sequence in a DNA construct, which method comprises the steps of a) providing each desired DNA unit to be assembled in the DNA construct, ***wherein each desired DNA unit has a restriction enzyme recognition sequence at its 5' end and a recognition sequence for the same restriction enzyme at its 3' end, said 3' recognition sequence also comprising a DNA methylase recognition sequence that is compatible with such a restriction***

*enzyme recognition sequence, and cleaving each desired DNA unit with said restriction enzyme, b) providing a starting DNA construct having an accessible restriction site for said restriction enzyme and cleaving the starting DNA construct with said restriction enzyme, c) inserting a first desired DNA unit provided in step a) into the DNA construct, thereby generating a ligated product, and bringing the ligated product into contact with a DNA methylase such that the restriction site at the 3' end of the first desired DNA unit in the ligated product is abolished, thereby generating a ligated product containing a DNA modification, d) cleaving the ligated product containing a DNA modification generated in step c) at an accessible unmodified recognition site for said restriction enzyme, e) repeating steps c) and d) with each subsequent desired DNA unit provided in step a), thereby generating a DNA construct containing all the desired DNA units in sequence.*

Applicants submit that, based on the teachings in Applicants' specification and the knowledge generally available in the art at the time of the invention, one of ordinary skill in the art would be able to make and use the claimed invention using only routine experimentation. Specifically, at, for example, page 7, line 20, through page 8, lines 1-21 of the specification, as well as in Examples 1 and 2 (pages 22-30 of the specification) Applicants teach suitable restriction enzymes and DNA modification enzymes for use in the claimed methods.

Moreover, Applicants respectfully submit that the predictability in the art is extremely high with respect restriction enzymes, DNA modification enzymes and the specific sequences recognized by such enzymes. Specifically, Applicants submit that one of skill in the art can readily determine whether the cohesive ends created by a particular restriction enzyme are compatible with the cohesive ends created by another restriction enzyme since the recognition sequences of such restriction enzymes are well characterized and known in the art. Similarly, one of skill in the art can readily determine whether a particular DNA modification enzyme is compatible with a particular restriction enzyme recognition sequence (or the sequence created by ligation of compatible restriction enzyme recognition sequences) since the recognition sequences of such DNA modification enzymes are also well characterized and known in the art (see, for example, New England Biolabs Catalog). The Examiner has also admitted at page 4 of the present Office Action, that the level of skill in the art is high. As such, and in view of the teachings in Applicants' specification, one of skill in the art would be able to practice the methods of the invention without undue experimentation.

Notwithstanding the foregoing, Applicants have amended the claims, thereby rendering this rejection of claims 1-3 and 5-8 moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection. Applicants wish to point out for the record that the claim amendments were made solely in the interest of expediting prosecution and allowance of the claims and in no way acquiescing to the validity of the Examiner's rejection.

***Rejections of Claims 1-17 and 21 Under 35 U.S.C. §112, Second Paragraph***

The Examiner has rejected claims 1-17 and 21 under 35 U.S.C. §112, second paragraph as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

With respect to claim 1, the Examiner is of the opinion that

[i]t is unclear that a desired DNA unit in step c) of the claim is identical to one of DNA units in step a) or not. Furthermore, it is unclear whether each subsequent desired DNA unit in step e) has identical properties as each DNA unit in step a).

Applicants respectfully submit that, in view of the amendments to claim 1, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection of claim 1 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 4, the Examiner is of the opinion that

[c]laim 4 recites the limitation "the desired DNA unit" in step c) of the claim. There is insufficient antecedent basis for this limitation in the claim because steps a) and b) only have DNA unit and have no desired DNA unit.

Applicants respectfully submit that, in view of the amendments to claim 4, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claim 4 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 8, the Examiner is of the opinion that

[c]laim 8 recites the limitation “the DNA modification” of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase “DNA modification” in claims 1-3.

Applicants respectfully submit that, in view of the amendments to claim 8, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that this rejection of claim 8 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

The Examiner is further of the opinion that claim 8 is “vague and indefinite” because it is unclear whether each subsequent desired DNA unit in step e) has identical properties as each DNA unit in step a) or not.

The Examiner refers to claim 8 in this rejection, however, since claim 8 does not have a step a) or a step e), Applicants assume that the Examiner intended to refer to claim 9. As such, Applicants have amended claim 9, thereby rendering the foregoing rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection to claim 9.

With respect to claim 9, the Examiner is also of the opinion that

[t]here is insufficient antecedent basis for this limitation in the claim because there is no phrase “other desired DNA unit” in step a) of the claim.

Applicants respectfully submit that, in view of the amendments to claim 9, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claim 9 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claims 9 and 10, the Examiner is of the opinion that

it is unclear that the ligated product in step d) is the ligated product in step c) or a ligated product in step d). Furthermore, since claim 9 or 10 does not indicate that a subsequent desired DNA unit in step d) has identical properties as a desired DNA unit in step b), it is unclear whether the ligated product in step d) can be cleaved with said first restriction enzyme or not.

The Examiner is further of the opinion that claims 9 and 10 are “vague and indefinite because it is unclear what each desired DNA in step e) represents for. Does each desired DNA in step e) represent for a desired DNA unit in step b) and a subsequent desired DNA unit in step d.”

Applicants respectfully submit that, in view of the amendments to claims 9 and 10, the foregoing rejections have been rendered moot. Accordingly, Applicants respectfully request that these rejections of claims 9 and 10 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.



**SUMMARY**

In view of the above amendments, Applicants believe that the present application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Applicants believe that no fee is due with this communication. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. SHW-009US from which the undersigned is authorized to draw.

Dated: November 27, 2006

Respectfully submitted,

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